

AMENDMENTS TO THE CLAIMS

1. (Original) A screening method for a compound, or a salt thereof, that promotes or inhibits the interaction between Rap1 and p30 and/or the binding of Rap1 with p30, which comprises:

(1) a process to allow

(a) a polypeptide selected from the group consisting of an active-form polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:2, an active-form polypeptide containing a point-mutated SEQ ID NO:2 amino acid sequence wherein the 12th glycine thereof is replaced with valine or an amino acid sequence essentially identical to said point-mutated amino acid sequence, a partial peptide thereof, and a salt thereof;

(b) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4, a partial peptide thereof, and a salt thereof; and

(c) a test sample

to come in contact with one another; and

(2) a process to detect the interaction and/or binding between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

2. (Original) The screening method according to claim 1, comprising:

(1) the process to allow a polypeptide selected from the group (a), a polypeptide selected from the group (b), and a test sample to come in contact with one another;

(2) the process to detect the occurrence of the interaction and/or binding between the polypeptide selected from the group (a) and the polypeptide selected from the group (b); and

(3) a process to select a compound that promotes and/or inhibits the interaction and/or binding between these polypeptides.

3. (Currently amended) The screening method according to claim 1 ~~or 2~~, wherein another peptide is fused to a polypeptide selected from the group (a) and/or a polypeptide selected from the group (b).

4. (Currently amended) The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b) is labeled and the label is detected or measured to detect the binding and/or interaction of the polypeptides.

5. (Currently amended) The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide of the group (b) bound to the polypeptide of the group (a) is assayed with a primary antibody against the polypeptide of the group (b) or a primary antibody against another peptide fused to the polypeptide of the group (b) to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

6. (Currently amended) The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (a) bound to the polypeptide selected from the group (b) is assayed with a primary antibody against the polypeptide of the group (a) or a primary antibody against another peptide fused to the polypeptide of the group (a) to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

7. (Currently amended) The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein the polypeptide selected from the group (b) bound to the polypeptide selected from the group (a) is assayed with a primary antibody against the polypeptide of the group (b) or a primary antibody against another peptide fused to the polypeptide of the group (b) and a secondary antibody against the primary antibody to detect the binding and/or interaction between the polypeptide selected from the group (a) and the polypeptide selected from the group (b).

8. (Currently amended) The screening method according to ~~any one of claims 1 to 3~~ claim 1, wherein

the polypeptide of the group (a) is an active-form fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:2 or an active fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine; and

the polypeptide of the group (b) is a polypeptide, or a salt thereof, wherein an Myc epitope is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:4.

9. (Original) A screening kit for a compound, or a salt thereof, which promotes or inhibits the interaction and/or binding between Rap1 and p30 which comprises an effective amount of

(a) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:2, and a polypeptide containing a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine, or an amino acid sequence essentially identical to said point-mutated amino acid sequence, a partial peptide thereof and a salt thereof; and

(b) a polypeptide selected from the group consisting of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4, a partial peptide thereof, and a salt thereof.

10. (Original) The screening kit according to claim 9, wherein another peptide is fused to the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b).

11. (Original) The screening kit according to claim 9, wherein the polypeptide selected from the group (a) and/or the polypeptide selected from the group (b) is labeled.

12. (Original) The screening kit according to claim 9, wherein
the polypeptide of the group (a) is a fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:2 or a fusion polypeptide, or a salt thereof, wherein glutathione-S-transferase is fused with the N-terminal side of a polypeptide having a point-mutated SEQ ID NO:2 amino acid sequence in which the 12th glycine thereof is replaced with valine; and

the polypeptide of the group (b) is a fusion polypeptide, or a salt thereof, wherein an Myc epitope is fused with the N-terminal side of a polypeptide having the amino acid sequence of SEQ ID NO:4.

13. (Currently amended) A compound, or a salt thereof, ~~with~~ which promotes or inhibits the interaction and/or binding between Rap1 and p30 and is obtained using the screening method according to claim 1 ~~or the screening kit according to claim 9.~~

14. (Original) The compound, or a salt thereof, according to claim 13 which inhibits the interaction and/or binding between Rap1 and p30.

15. (Original) A pharmaceutical composition containing the compound or the salt thereof according to claim 13.

16. (Original) A pharmaceutical composition comprising an effective amount of the compound, or a salt thereof, according to claim 14.

17. (Currently amended) The pharmaceutical composition according to claim 15 ~~or 16~~, wherein a target to be treated or prevented is selected from the group consisting of:

- (a) inflammatory diseases;
- (b) immune diseases;

- (c) graft versus host reaction upon organ transplantation; and
- (d) cancers.

18. (Original) A monoclonal antibody that recognizes a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4.

19. (Original) A diagnostic method which comprises using the monoclonal antibody according to claim 18.

20. (Original) A diagnostic kit which comprises an effective amount of the monoclonal antibody according to claim 18.

21. (Original) A polypeptide, or a salt thereof, that functions intracellularly against a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:4 in a dominantly negative fashion.

22. (Original) A composition comprising an effective amount of the polypeptide, or a salt thereof, according to claim 21 for treatment or prevention of a disease selected from the group consisting of:

- (a) inflammatory diseases;
- (b) immune diseases;
- (c) graft versus host reaction on organ transplantation; and
- (d) cancers.

23. (Original) A polynucleotide encoding the polypeptide according to claim 21.

24. (Original) A composition comprising an effective amount of the polynucleotide according to claim 23 for treatment or prevention of a disease selected from the group consisting of:

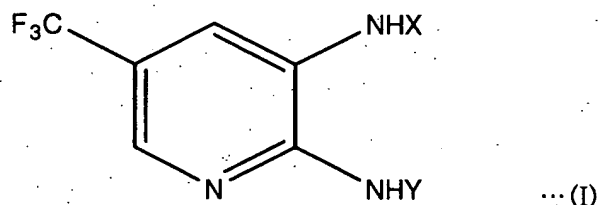
- (a) inflammatory diseases;
- (b) immune diseases;
- (c) graft versus host reaction upon organ transplantation; and
- (d) cancers.

25. (Original) A transgenic animal having a regulated expression of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:10.

26. (Original) The transgenic animal according to claim 25, wherein a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO:10 is overexpressed.

27. (Currently amended) The transgenic animal according to claim 25 or 26, which is a mouse.

28. (Original) A Rap1-p30 binding inhibitor which comprises an effective amount of a compound, or a salt thereof, of the formula (I):



wherein X is a group: $-CW^1R^1$ or $-C(=W^1)W^2R^2$

in which

R^1 is alkyl, haloalkyl, alkoxy carbonylalkyl, alkenyl, haloalkenyl, alkenyl

substituted with thienyl, cycloalkyl, cycloalkyl substituted with a halogen atom, phenyl, phenyl substituted with a halogen atom, phenyl substituted with alkyl or haloalkyl, phenyl substituted with alkoxy or haloalkoxy, tetrahydronaphthyl, indanyl, furanyl, or thienyl,

R^2 is alkyl or haloalkyl, and

W^1 and W^2 each independently represents an oxygen or sulfur atom, and

Y is $-SO_2R^9$

in which

R^9 is alkyl, haloalkyl, phenyl, phenyl substituted with a halogen atom, phenyl substituted with alkyl or haloalkyl, or phenyl substituted with alkoxy or haloalkoxy].

29. (Original) The Rap1-p30 binding inhibitor according to claim 28, wherein X is alkoxycarbonylalkylcarbonyl, alkenylcarbonyl, alkenylcarbonyl substituted with thienyl, cycloalkylcarbonyl, indanylcabonyl, furancarbonyl, thiophenecarbonyl, tetrahydronaphthylcarbonyl, or benzoyl unsubstituted or optionally substituted with a halogen atom or haloalkyl, and Y is alkylsulfonyl.

30. (Original) The Rap1 and p30 binding inhibitor according to claim 28, wherein X is cycloalkylcarbonyl, furancarbonyl or benzoyl unsubstituted or optionally substituted with halogen, and Y is alkylsulfonyl.

31. (Original) The Rap1-p30 binding inhibitor according to claim 28, wherein the compound is selected from the group consisting of

N-(2-ethylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclohexanecarboxamide,
N-(2-methylsulfonylamino-5-trifluoromethyl-3-pyridyl)-4-fluorobenzamide,
N-(2-isopropylsulfonylamino-5-trifluoromethyl-3-pyridyl)-3-fluorobenzamide,
N-(2-methylsulfonylamino-5-trifluoromethyl-3-pyridyl)-2-furancarboxamide, and
N-(2-isopropylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclopentanecarboxamide.

32. (Original) A Rap1-p30 binding inhibitor comprising an effective amount of N-(2-ethylsulfonylamino-5-trifluoromethyl-3-pyridyl)cyclohexanecarboxamide or a salt thereof.

33. (New) A compound, or a salt thereof, ~~wich~~ which promotes or inhibits the interaction and/or binding between Rap1 and p30 and is obtained using the screening kit according to claim 9.